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XANTHELASMA AND CHRONIC JAUNDICE.[1]

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Xanthelasma, xanthoma multiplex, or vitiligoidea as an accompaniment of chronic jaundice is a comparatively rare affection. This paper is based on three such cases admitted to Dr. Osler's wards at the Johns Hopkins Hospital. These constitute all the cases that have occurred in the hospital during the first sixteen years ending with May 15, 1905. During this period there had been 18,400 medical admissions, among which there was a large number with chronic icterus. All three cases were admitted between January 30 and June 26, 1901, two having been under observation in the same ward at the same time. The main points in the clinical histories of the cases follow:

Case I. (*Gen. Hosp. No.* 33,689).—*History of typhoid fever; later, cholecystitis; onset of symptoms of gallstones of the common duct two years after the typhoid infection; eight months after the onset of the jaundice the xanthoma plaques made their appearance; xanthomata on gums; exploratory laparotomy; gallstones in the gall-bladder and common duct; spontaneous disappearance of the xanthelasma after leaving the hospital.*

L. J. F., female, white, married, aged thirty-nine years, was admitted to the Johns Hopkins Hospital on January 30, 1901, complaining of "jaundice."

The family history was unimportant, with the exception that her father had had three attacks of jaundice associated with enlarged liver, attributed to the use of alcohol.

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[1] Read before the Association of American Physicians, Washington, D. C., May, 1905.

The patient was healthy as a young woman. Married twenty-one years. One child eighteen year ago. Typhoid fever in June, 1897, about three and one-half years before admission. Attack lasted five weeks. After temperature returned to normal, but before she was out of bed, she had a very severe attack of pain in the epigastrium, associated with vomiting. There was great sensitiveness in the upper abdomen, with fever of several days' duration.

The present illness dated from the summer of 1899, two years after the typhoid infection. It began with an attack of abdominal pain, without jaundice. In December, 1899, thirteen months ago, she had several attacks of colicky pain in the epigastrium, after which she became jaundiced. These were accompanied by chills, fever, and sweating. The epigastrium was described as being swollen and very sensitive. From that date there had been repeated attacks of the same character. Jaundice had been persistent, but varying somewhat in intensity. The stools were intermittently clay-colored. Patient lost fifty-three pounds in thirteen months.

The jaundice had existed for thirteen months. There had been severe pruritus. Five or six months ago, and eight months after the onset of the jaundice, she first noticed flat, yellow patches appearing on the palms of the hands, particularly in the folds of skin at the flexures of the joints. Later others appeared in the folds of the elbows, over the olecranon processes, axillæ, sides of the neck, and dorsal surfaces of the toes. At first flat, they subsequently became somewhat raised. The patches over the olecranon processes were sensitive on being struck, and those on the hands were also tender when she used the broom. Friction seemed to favor their occurrence. One particularly thick xanthoma patch developed beneath a ring on the third finger of the left hand. The finger became so sensitive that the ring had to be removed.

Physical Examination. The following were the essential features in the physical examination on admission: Patient still fairly well nourished. Uniformly jaundiced; sclerotics deep yellow in color.

Distribution of Xanthoma Plaques. One very small one on left upper eyelid. Large, flat, yellow patch on right side of neck, 3 x 4 cm. in diameter, with small outlying portions. Similar but still larger one on right side of neck. Smaller one over the fold of left trapezius muscle. *Right arm and hand.* Patch in fold of axilla. Areas of keratosis about elbow and numerous nodular xanthomata around them. Exactly corresponding to the fold of the elbow there was a long linear xanthoma, with small outlying ones. Small patch over one of the creases at the wrist. Two in the palm of the hand over palmar creases. In the creases on the flexor surfaces of all the metacarpo-phalangeal and nearly all the interphalangeal joints there were xanthoma plaques, usually linear, but occasionally irregular in outline. A few patches were scattered over the sides of the fingers and on the knuckles. *Left arm and hand.* The distribution of the lesions was so nearly identical with those on the right upper extremity that a separate detailed description is unnecessary. A few patches on the upper chest. None on abdomen. Few on dorsal surface of the toes. All the patches had a distinct whitish-yellow tint, differing materially from the color of the jaundiced skin. The majority of the xanthomata were flat and not elevated. A few of the older ones were elevated and slightly nodular, particularly those on the extensor surfaces of the elbows.

The examination of the thoracic organs revealed nothing of importance. The liver was considerably enlarged. The absolute hepatic flatness extended 6.5 cm. below the costal margin in the mammillary line, and 13.5 cm. below the tip of the ensiform in the median line. The gall-bladder was not palpable. The splenic border was rounded and palpable 5.5 cm. from the costal margin.

The stools were light in color, but contained some bile. Urine contained bile pigments. Blood coagulation time on admission was eight minutes and fifteen seconds.

On January 31st Dr. Osler made the following notes: "Interesting points in connection with the case are: (1) sequence of typhoid, cholecystitis, and gallstones; (2) chronic jaundice associated with delayed coagulation time; (3) chronic jaundice associated with the symptom-complex of gallstone in the common duct; (4) xanthelasma.

On February 1st I noted that there was apparently the same sort of lesion on the gums as was found on the extremities. The patches had an opaque yellow appearance and were slightly thickened. The lesion was most evident on the gum over the upper incisors and on that over the lower incisors and canines.

On February 27th a few fresh xanthoma patches were noted for the first time over the patient's back. Under the administration of calcium chloride the coagulation time of the blood became reduced to three minutes and fifty-five seconds.

Operation. On February 28th Dr. Halsted performed an exploratory laparotomy, and found two large stones in the gall-bladder and one in the common bile-duct. There were no indications of xanthomata in the mucous membrane of the gall-bladder or bile-duct.

The patient did well until the eighth day, when she had a severe secondary hemorrhage from the wound. Later she developed a fibrinous pleurisy and a pericarditis, from which she eventually recovered, and was discharged from the hospital much improved, but still somewhat jaundiced, on June 1, 1901.

Dr. Florence Sabin, who was Medical Interne in charge of the patient when she was in the hospital, followed the subsequent progress of the case and she has kindly turned over the notes to me. These may be briefly summarized as follows:

April 7, 1903. General health excellent; still jaundiced. Operation wound healed after eighteen months. Had occasional attacks of soreness over the liver region, which lasted a few days, during which time the urine becomes very dark.

March 9, 1905. Patient wrote that she was in excellent health and weighed 150 pounds. In reply to a question as to the present condition of the yellow patches she stated that they had entirely disappeared.

In this case the xanthomata were mainly of the flat variety, although there were a few of the nodular variety about the right olecranon. The jaundice had been present for eight months before the onset of the xanthomata. An interesting feature of the case was the spontaneous disappearance of the xanthomata after the patient left the hospital.

CASE II. (*Gen. Hosp. No.* 33,912).—*Gallstones of the common and hepatic ducts and of the gall-bladder; biliary hypertrophic cirrhosis; jaundice of ten years' standing; appearance of xanthomata eight years after the onset of the jaundice. Severe hemorrhages from the nose and uterus; death and autopsy.*

M. A. C., female, white, married, aged thirty-nine years, was admitted to the Johns Hopkins Hospital on February 19, 1901, complaining of hemorrhages.

The family history was unimportant. The patient had always been a healthy woman previous to the onset of the present illness. She was the mother of six children.

The present illness began ten years ago with what she described as "malaria." She had attacks characterized by chills, fever, sweating, and paroxysmal pain in the right hypochondrium at the beginning of the attacks. Jaundice developed at the onset and has since continued with varying degrees of intensity. The attacks of pain, chills, and fever have recurred at intervals up to the present. In March, 1900, she had severe hemorrhages from the nose and uterus, which lasted three weeks. Four days before entrance these recurred and became so severe that she sought admission to the hospital for them. For years "blood blisters" the size of a split pea had appeared over the body, and she was liable to have bruises develop on the slightest injury.

Two years ago, and eight years after the onset of the jaundice, she noticed yellow patches developing on the palms of the hands and subsequently on other parts of the body. There were no symptoms referable to them.

Physical Examination. The following were the essential features in the examination: The patient was fairly nourished. There was intense jaundice and extreme pallor of the skin and mucous membranes. The patient was very freckled. The lungs were clear on percussion and auscultation. The heart showed nothing of importance excepting a faint systolic murmur, probably anæmic in origin, at the mitral area. The relative liver dulness began at the fifth rib in the mammillary line; the absolute at the sixth rib in the same line not extending quite to the costal margin. Just below the costal margin and inside the mammillary line there was an indefinite rounded mass to be felt, which descended on inspiration and suggested possibly a distended gall-bladder.

Xanthomata. On both of the upper and lower eyelids were long, somewhat raised yellow plaques. In the lines of the palmar surface of both hands and along the sides of the fingers were similar plaques, only less raised. The elbows, both flexor and extensor surfaces, and the axillæ had small rounded tumor-like nodules. Over both buttocks were numerous larger, round, raised, nodular, yellow masses, varying up to 0.5 cm. in diameter. There were a few over the knees and dorsal surfaces of the feet.

There was a spontaneous subcutaneous hemorrhage over the right knee, and a continuous flow of pale bloody fluid from the vagina.

The urine contained abundance of bile pigments, a trace of albumin, but no casts.

On admission the red cells were 1,880,000 per c.mm.; the leukocytes, 15,700 per c.mm.; and the hæmoglobin, 23 per cent. The coagulation time was fourteen minutes. Under complete rest and the administration of iron the patient's condition markedly improved. On March 25th the blood count was as follows: red cells, 4,804,000 per c.mm.; leukocytes, 9700 per c.mm.; hæmoglobin, 58 per cent. Under calcium chloride the coagulation time on this date had become reduced to four minutes and fifty-three seconds. Her condition continued to improve and she progressively gained in weight. She refused an exploratory operation, and, at her own request, was discharged on April 18, 1901.

A few days after her discharge from the hospital the patient died, death having been preceded by severe uterine hemorrhages. Permission was obtained for an autopsy, which was made by Dr. W. G. MacCallum.

Anatomical Diagnosis. Cholelithiasis; obstructive jaundice; biliary hypertrophic cirrhosis of the liver; splenic tumor; acute nephritis; ovarian cystomata; xanthelasma multiplex.

The following were the chief features about the liver and bile passages: The common duct was plugged with a large plum-shaped gallstone. There were several gallstones in the gall-bladder, almost embedded in saccules in the bladder wall. The hepatic duct was filled by a curved cylindrical concretion. Above this the gall-ducts throughout the liver were enormously thickened. The walls of the ducts were almost 0.5 cm. in thickness and of a deep yellow color. On section of the liver the bile-ducts stood out everywhere looking like sclerotic arteries. There were some minute yellow flecks in the mucosa of the walls of the bile-ducts, but there were no lesions typical of xanthomata. The liver was large and measured 35 x 18 x 11 cm., and weighed 2800 grams.

The chief features of interest in this case were: 1. The combination of cholelithiasis, with biliary hypertrophic cirrhosis as a cause of the jaundice. 2. The development of the xanthomata only after the jaundice had existed for eight years. 3. The xanthomata were of two types—flat and nodular.

CASE III. (*Gen. Hosp. No.* 35,296).—*Hypertrophic cirrhosis of the liver; severe uterine hemorrhages; jaundice lasting one and a half years before the onset of the xanthomata; hemorrhages from the gums and uterus.*

L. H., female, white, married, aged forty-two years, was transferred from the surgical to the medical department of the Johns Hopkins Hospital on June 26, 1901, complaining of "liver trouble and jaundice."

With the exception of her father and mother having both died of tuberculosis the family history was unimportant. The patient had had six children and one miscarriage. She had been in the habit of taking an occasional glass of beer or porter for years; no whiskey. For several years she had suffered from attacks of abdominal pain, particularly after indiscretions in eating.

She dated her present illness from five years ago, when she began to have vertigo and general weakness and was forced to give up her work. Her bowels, which had been previously constipated, became rather loose. Two and one-half years ago jaundice developed, which had continued ever since. The stools were gray and the urine high colored. There had been no chills, fever, or attacks of abdominal colic, although she had had indefinite pains in the left hypochondrium. For a year she had noticed a tender spot over the liver, the sensitiveness increasing with pressure or deep inspiration. For the same period she had suffered from repeated attacks of severe uterine hemorrhages. On November 19, 1900, she was admitted to the surgical side of the hospital. She was then jaundiced. The red blood cells were 1,504,000, per c.mm., and the hæmoglobin 28 per cent. The coagulation time was between three and four minutes. Owing to the severe anæmia an exploratory laparotomy seemed inadvisable. Her general blood condition gradually improved, and on May 31, 1901, Dr. Mitchell performed an exploratory laparotomy. Careful examination of the bile passages failed to reveal any gallstones. The liver was much enlarged and presented the appearances of an hypertrophic cirrhosis, which was the surgical diagnosis. The post-operative history was uneventful, and the wound healed well. The jaundice persisted, however, and on June 26, 1901, she was transferred to the medical side of the hospital.

For about one year previous to her admission to the medical ward she had noticed whitish-yellow spots appearing, one below the left eye, the other below the right. These had been gradually increasing in size.

Physical Examination. The patient was of small stature, but was fairly well nourished. Jaundice was intense. The lungs were normal. Over the apex of the heart was heard a loud blowing systolic murmur, which was transmitted to the axilla, and was also audible over the body of the heart. The liver dulness was considerably increased and extended about 6 cm. below the costal margin in the right mammillary line. The border could not be distinctly felt, owing to the tenderness over the hepatic region. There was considerable tympanic distention of the abdomen; but no ascites. The spleen was not palpable.

Situation of the Xanthomata. Over the lower right eyelid there was a flat yellow xanthoma patch measuring 1 cm. x 2 mm. Above and within the left internal canthus there was a similar one measuring 1.5 cm. in diameter. Careful search failed to reveal any xanthomata on any part of the body.

The urine contained abundance of bile pigments, but no albumin or casts were present.

During her stay on the medical side she had some bleeding from the lips and mucous membrane of the mouth. On July 4, 1901, she was discharged from the hospital at her own request.

The patient returned to the hospital for observation on November 28, 1904. The jaundice was still present. She had had some bleeding from the gums and from a scratch on the ear. The liver border was palpable three fingers' breadth from the costal margin.

In this case the xanthomata were confined to the eyelids. The patient gave a definite account of their appearing one and a half years after the onset of the jaundice. The case was therefore not one in which a patient with xanthomata of the lids developed a chronic jaundice, but the reverse. Although the xanthomata were not so widely distributed as in the previous cases, yet there was no reason to doubt that they were dependent on the hepatic disease or the jaundice.

Xanthelasma is not a common disease under any circumstances. The cases in which it is limited to the eyelids (*xanthoma palpebrarum*) occur much more frequently than those where the lesions are more generally distributed (*xanthoma multiplex*). The majority of the latter form are of congenital origin in the young, or associated with jaundice or glycosuria in adults.

Xanthomata occur in two forms, either as flat plates or plaques (*xanthoma planum*), or as nodules or tumors (*xanthoma tuberculatum* or *tuberosum*). According to Crocker they represent little more than differences in position, shape, and degree of development.

Xanthoma palpebrarum constitutes the bulk of the cases, and the lesion here is in the form of *plaques*. It commences most frequently on the left upper eyelid near the inner canthus, and may form a semicircle of the whole eye. Later the right side becomes affected and the lesion is usually symmetrical. The patches have a chamois-leather yellow color. They are either not at all or only slightly raised and are situated in the corium. They are soft and smooth and the skin does not seem thickened when it is picked up.

Xanthomata when of the *nodular* variety have the same color as the plaques, but project more or less above the surface. They vary in size from a millet-seed to a large pea, and in rare instances may be 2 or 3 cm. in diameter. The small ones are convex, round or oval, and often have a fine network of capillaries over them. They are soft and smooth to the touch. The larger ones are made of conglomerations of the smaller ones, and are irregular in contour and are more or less firm in consistence, depending upon the amount of connective tissue they contain.

Xanthoma multiplex in the adult is most frequently associated with jaundice of long standing, and it is this form with which we are especially interested in this paper. The first reference I have been able to find of the association of xanthelasma with chronic jaundice is in a paper by Thomas Addison and William Gull,[1] published in 1851, and entitled "On a Certain Affection of the Skin, Vitiligoidea—*a*, Plana, *β*, Tuberosa. With Remarks and Plates." They report five cases of a skin affection with which they were not familiar, and, owing to a certain resemblance between it and the disease described by Willan as vitiligo, they suggested the name *vitiligoidea.* They distinguished two varieties of the affection: the flat, to which they gave the name *vitiligoidea plana,* and the nodular, which they designated by the name *vitiligoidea tuberosa.* Of the five cases three were in patients with chronic jaundice. In one of the three the lesions were distributed in the creases of the wrists, hands, and interphalangeal joints, similar to the distribution in Cases I. and II.

The lesions of xanthoma multiplex in chronic jaundice are both in plaques and nodules, the former type prevailing. They may involve the skin, mucous and serous membranes, and the tendons. The commonest positions are the eyelids, where it is said to most often begin, the palms and soles and backs of the hands and feet, flexures of the wrists, and the buttocks in and near the cleft and about the anus. It is of interest to note that in Cases I. and II. the xanthomata made their appearance first on the palms of the hands. The plaques are most commonly found on the eyelids, joint flexures, and mucous membranes. In Case I. the gums were affected. In Case II. there were suggestive indications of xanthomata in the mucous membrane of the bile-ducts on macroscopic examination, a suspicion which was confirmed on microscopic study of the sections. The nodules usually occur on the extensor aspects of the joints, particularly on parts exposed to irritation, as the knuckles, elbows, and knees. In xanthoma multiplex symmetrical arrangement of the lesions is the rule, and is often very striking. This was a marked feature of Cases I. and II., and was also true in Case III., in which the lesions were limited to the eyelids. The xanthomata appear gradually and are slow in their development. After months or years their growth ceases, and there is usually no future change in them. Crocker states that three instances have been reported in which spontaneous disappearance occurred after several years. In Case I. the xanthomata had entirely disappeared within four years after the patient left the hospital, and about four and a half years after their first appearance.

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[1] Guy's Hospital Reports, new series, 1851, vol. vii. p. 265.

The xanthomata rarely cause any inconvenience excepting from their disfigurement. Occasionally, burning, prickling, or itching have been experienced, and when they have occurred on the palms of the hands or knees, grasping objects or kneeling may cause some discomfort, or even pain.

In 1882 a committee composed of Jonathan Hutchinson, Alfred Sangster, and H. Radcliffe Crocker[1] was appointed by the London Pathological Society to report on 2 cases of xanthoma multiplex, one of which was demonstrated before the Society by Stephen Mackenzie, and the other by James Startin. They collected data of 23 cases of xanthoma multiplex in adults with jaundice; 10 of these were in males, 12 in females, and in 1 the sex was not stated. It would seem, therefore, that women are a trifle more liable to the affection than men. They also found records of 5 cases of xanthoma multiplex in adults without jaundice; 4 of these were males and 1 a female. Statistics of 8 cases of xanthoma multiplex, either congenital or commencing before puberty, were also collected from the literature. It was not possible to definitely ascertain the sex in these cases, but 4 were believed to be males and 4 females.

Some of the conclusions of this committee regarding xanthoma multiplex were as follows: 1. That cases occurring before puberty, although structurally the same as those beginning at a later period, are etiologically different, have no traceable connection with hepatic disease, but are probably to some extent hereditary. That they may be congenital, and that the eyelids always escape. 2. That four-fifths of the cases of xanthoma commencing after puberty are associated with chronic jaundice from obstruction of the bile-ducts. That in some of the others the health has been perfect, but that diabetes has been observed more than once. That the eyelids are almost always involved and almost invariably the starting point. Occasionally spontaneous involution occurs. That, as regards sexes, the numbers affected are nearly equal.

From the standpoint of *etiology* there seems little doubt but that the jaundice is the exciting agent in the xanthoma multiplex cases accompanied by this symptom. The hepatic conditions causing the jaundice have been found to be cholelithiasis, stricture of the bile-ducts, atrophic and hypertrophic cirrhosis of the liver, hydatids, and cancer. How the jaundice acts in effecting the changes in the corium is not known, but presumably it is through the agent of a toxin. Besnier, Hollopeau, and Kaposi regard the jaundice and liver troubles as secondary, and due to the development of the xanthomata in the viscera. Crocker states that the order of development of the clinical features does not support this view. It may be of interest here to note that Besnier and Gailleton have described a condition in hepatic affections which they call *xanthochromia* of the skin, and not due to jaundice in some cases. It is more marked on the face and trunk than on the extremities, the conjunctiva and buccal mucous membrane are uncolored, and there is no bile in the urine and feces.

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[1] Transactions of the Pathological Society of London, 1882, vol. xxxiii. p. 376.

There is considerable difference of opinion as to the *pathology* of this skin affection. Xanthomata were excised from Cases I. and II., and the sections were carefully studied by Dr. W. W. Williams, of the Harvard Medical School, whose report has not yet appeared, but who has kindly furnished me with a copy of his histological examination. In association with these cases, sections from a xanthoma palpebrarum complicating a case of diabetes insipidus, admitted to the Johns Hopkins Hospital and reported by me before this Association last year, were also studied. The findings in all three cases were practically identical, and I quote briefly the main features of Dr. Williams' report:

"The epidermis is essentially normal, although in places there are large vacuolated cells in the lower part. Below this is a layer of practically normal connective tissue, which, however, contains a few pigmented spindle-shaped cells. Branching off from this layer are numerous larger and smaller fibrous bands, becoming continuous with the normal tissue deeper down, and forming an irregular network. These trabeculæ are composed of fibrous connective tissue, with a few deeply staining, long, narrow nuclei and some delicate elastic fibres. Also a few delicate pigment granules are to be seen.

"Within the meshes of this fibrous reticulum are masses of pale cells, although in places the same pale cells occur singly or in pairs between the connective-tissue fibres. Surrounding each cell in these groups is a delicate reticulum containing here and there fine elastic fibres.

"These pale cells (so-called xanthoma cells) vary much in size; and though some are small and mononuclear and others large and multinuclear, they are all otherwise similar. There is no definite cell membrane, and the protoplasm is everywhere finely granular and contains more or less refractive granules, which react to the fat stains. Some of the cells are vacuolated, and others definitely phagocytic.

"The nuclei are, as a rule, oval, with a distinct membrane, vesicular, and often contain several nucleoli. They are usually more or less centrally situated. Mitosis is seen in some of these pale granular cells. The number of nuclei vary from one to twenty.

"About some of the bloodvessels, traversing these groups of cells, slight lymphoid cell infiltration has taken place. The endothelium of some of these vessels and of many lymph spaces is swollen and contains fatty granules. Also in the perivascular lymph spaces are seen pale, granular, vesicularly nucleated cells. In none of the specimens were any polymorphonuclear leukocytes, nerves, or muscle cells found, or any involvement of the hair follicles or sebaceous or sweat glands noticed."

Dr. Williams' report on the histological examination of the bile-ducts in Case II., which came to autopsy, is exceedingly interesting. "The walls of the bile-ducts are considerably hypertrophied, containing many elastic fibres, and the lumena are lined with a mass of lymphoid and plasma cells, and also many large, pale, granular, vesicularly nucleated cells, similar to those already described in the skin lesions." Apparently these changes were regarded as due to the development of xanthomata in the bile-ducts.

In a communication from Dr. Williams he wrote: "In my conclusions on these growths I maintained that they were of endothelial origin, though many described in the literature, and also one I described as really lipomata—lipoma xanthomatodes."

The description given by Crocker[1] and Touton for sections of xanthoma palpebrarum agree closely with Williams' report. There is no essential difference between the plaques and the nodular variety. In the latter the bulk of the lesion is more superficial, and is in the papillary layer pushing up the epidermis above the level of the surrounding surfaces. The connective tissue is much more abundant than in the case of the plaques, and is most marked about the hair follicles and sebaceous glands. The fatty masses are less conspicuous and yellow oil globules infiltrate the meshes between the fibrous tissue. Crocker holds that in the development of the xanthomata inflammation is the primary factor; that the xanthoma cells and the connective-tissue growth are secondary, and that the whole process is of toxæmic origin.

Köbner thinks that the lesions are derived from embryonic remnants. Török claims that the xanthoma plaque is composed of adipose cells interrupted in their progress to complete evolution, and that it is not a tumor, but an excess of growth. Unna holds that the fat in xanthoma palpebrarum is a sort of fatty infiltration of the orbicularis muscle, the fat being in the lymph spaces and the giant cells being sections of dilated lymphatics. Pollitzer claims that the eyelid lesion is the product of the degeneration of embryonically displaced muscle fibres. This view has not been supported and seems to be disproven by the clinical fact that in both children and adults, after the lesion begins on the eyelids, it subsequently makes its appearance on various parts of the body.

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[1] Diseases of the Skin, third edition, p. 745.

There is no special difficulty in making a *diagnosis*. About the only condition likely to be confused with it is *milium palpebrarum*. These are usually small and situated near the inner canthus of the upper lid. Being due to retained sebaceous secretion, they are generally white, and occasionally the dark-colored opening of the duct may be seen. Milium is more superficial and firmer, and the contents of the nodule can easily be peeled out. Politzer refers to cases of *multiple dermoid cysts* of the skin, in which the diagnosis was possible only on microscopic examination of excised tissue.

After developing gradually for years the xanthomata become stationary and persist in the majority of cases throughout life. In rare instances, as in Case I., spontaneous involution may occur. In this case operation had been performed with a relief of the gallstone symptoms and almost complete disappearance of the jaundice.

There is practically no treatment for the condition, excepting incision, that yields results. It seems almost certain that the xanthomata are due to the jaundice or to some associated toxic substance circulating in the blood. Consequently efforts should be made to relieve the causes of the jaundice, which is possible at least in the cases of cholelithiasis.

SUMMARY. The three cases here reported were all in women, their respective ages being thirty-nine, thirty-nine, and forty-two years. The duration of the jaundice before the xanthomata appeared was eight months, eight years, and one and one-half years. The cause of the jaundice was gallstones of the common duct in two cases, one of which also had biliary hypertrophic cirrhosis of the liver, and in the third case hypertrophic cirrhosis of the liver alone. In all three cases the eyelids were involved, in one these only. In the other two there were lesions on the extremities and to a less degree on the trunk. In two cases the xanthomata appeared on the hands first; in the third on the eyelids. The xanthomata were chiefly in the form of plaques in all the cases. There were a few nodular xanthomata in Cases I. and II. The distribution was strikingly symmetrical. In Case I. there were xanthomata on the gums, and in Case II. histological examination of the bile-ducts showed that xanthomata of the mucous membranes of the ducts were present. At all events, the histological picture showed cells identical with the "xanthoma cells" of the lesions in the skin. In Case I. there was a spontaneous disappearance of the xanthomata four and one-half years after their onset, and about four years after the gallstones were removed at operation. Two of the cases were operated on, and one came to autopsy, so that the causes of the jaundice were definitely ascertained.

Four-fifths of the cases of xanthoma multiplex in adults occur in chronic jaundice. In these cases men and women are about equally affected, with possibly a slightly greater frequency in the latter. The hepatic conditions causing the jaundice have been found to be gallstones, stricture of the bile-ducts, atrophic and hypertrophic cirrhosis of the liver, hydatids, and cancer. In addition to the skin, the tendons and mucous membranes may occasionally be involved. The onset is said to be most frequently on the eyelids. The xanthomata accompanying jaundice are believed to be directly traceable to the latter or to some associated toxic substance circulating in the blood. Symmetry in distribution is often striking, and the tendency to develop in the folds and creases of the joints is a remarkable feature. The views as to the actual nature and sequence of tissue changes in the lesions vary much. Crocker thinks that inflammation is the primary factor and that the xanthoma cells and connective-tissue growth are secondary, and that the whole process is of toxæmic origin. Williams' careful histological study indicates strongly that the xanthomata are of endothelial origin. Once they develop they rarely disappear. Spontaneous involution is rare. No treatment other than surgical in suitable cases is of any avail. The indications are to relieve the underlying process if possible.

THE NATURE AND THE LESIONS OF CIRRHOSIS OF THE LIVER, WITH SPECIAL REFERENCE TO THE REGENERATION AND REARRANGEMENT OF THE LIVER PARENCHYMA.[1]

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The study of cirrhosis of the liver has been approached from several points of view—etiological, anatomical, and clinical; but since the disorder was first described by Vesalius special interest has centred in the obvious and most conspicuous feature of the lesions—the fibrosis; so much so, indeed, that the term "cirrhosis," first employed by Laennec to describe the yellowish (κιῤῥός) "hobnails," which he regarded as new-growth, has by a curious transference of meaning become almost inseparable from, with some writers practically identical with, the sclerotic process; and, indeed,

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[1] Read before the Association of American Physicians, Washington, D. C., May, 1905.